SUPPORT FOR THE AMENDMENT

Support for the amendment to claim 1 is found on page 11,lines 17-22 of the specification and examples 1-2 in which commercially available YMC Pack Sil S-5, YMC Pack Sil and YMC-SIL-120-S15/30 are used. "Pack Sil" is a term used by the YMC company to describe columns containing ultra high-purity silica (see attached web site page). No new matter would be added to this application by entry of this amendment.

Upon entry of this amendment, claims 1-8 will remain active in this application.

REQUEST FOR RECONSIDERATION

The claimed invention is directed to a method for producing alkyl (3R, 5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3, 5-dihydroxy-6-heptenoate by epimeric separation by liquid chromatography treatment using silica gel as the packing material.

Applicants wish to thank examiner Seaman for the helpful and courteous discussion held with their U.S. representative on December 18, 2006. At that time, applicants' U.S. representative argued that the cited references failed to describe uncoated silica gel and that the use of uncoated silica gel was clear from applicants' disclosure. The following is intended to expand upon the discussion with the examiner.

The claimed invention is directed to a method for producing alkyl (3R, 5S)-7-[2-cyclopropyl-4-(4-fluorophenyl)quinolin-3-yl]-3, 5-dihydroxy-6-heptenoate by epimeric separation by liquid chromatography treatment using **uncoated silica gel** as the packing material.

The rejections of claims 1-5 and 7 under 35 U.S.C. §102(a) and (b) and of claim 6 under 35 U.S.C. §103(a) over Ikeda et al., U.S. 5,939,552, Nagamatsu et al. (1999), Chen et al., U.S. 6,835,838 and Onishi et al., U.S. 6,946,557 are respectfully traversed.

None of the cited references discloses or suggests a method for producing the claimed compound by using uncoated silica gel as the packing material in a liquid chromatography.

Ikeda et al. describes optical resolution of a racemic mixture of an optically active mevalonolectone compound by means of a batch system chromatography which uses a column filled with a filler selected from a group consisting of particles of polysaccharide ester derivative, particles of a polysaccharide carbamate derivative and particles of a support which carries a polysaccharide ester derivative and/or a polysaccharide carbamate derivative (column 1, lines 51-58). This described a coating and support structure. The reference makes clear that the polysaccharide derivative is the solid support and that silica gel, amongst others may be used as a support for the polysaccharide derivative (column 6, lines 25-35). The reference fails to describe uncoated silica gel as the packing material.

Nagamatsu et al. describes separation of DOLE **racemic mixture** on slightly modified Chiralcel OF, 20μm (Daicel) (page 58, section 2.5. Columns). Chiralcel OF is cellulose tris (4-chlorophenyl carbamate) **coated on a silica gel** substrate. Chiralcel OF is not uncoated silica gel as the packing material.

Chen et al. at column 16, describe the use of Chiralpak AD. Chiralpak AD is amylose tris (3,5-dimethylphenyl carbamate) **coated on a silica-gel** substrate. Chiralpak AD is not uncoated silica gel as a packing material in a liquid chromatography treatment.

Onishi et al. describe the use of cellulose tris (4-chlorophenyl carbamate) supported on a carrier as a filler for liquid chromatography. Cellulose tris (4-chlorophenyl carbamate) is Chiralcel OF, and as discussed above is not uncoated silica gel as the packing material.

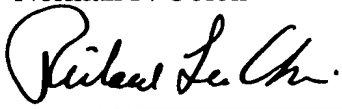
None of these chromatography supports are uncoated silica gel as a packing material. Applicants note that the claims have been amended to recite uncoated silica gel. Such amendment is clear from applicants' use of the Pack Sil ultra high purity silica columns of YMC company. To the contrary, the packing materials are a polysaccharide ester derivative

and/or polysaccharide carbamate derivative which are **coated onto the surface of a silica gel**. There is no exposed surface of silica gel in these packing materials such that the silica gel is not a liquid chromatography packing material. Since the cited prior art fails to disclose or suggest the use of uncoated silica gel, the claimed invention is neither anticipated nor rendered obvious from these references and withdrawal of the rejections under 35 U.S.C. §102(a, b) and 35 U.S.C. §103 (a) is respectfully requested.

Applicants submit that this application is now in condition for allowance and early notification of such action is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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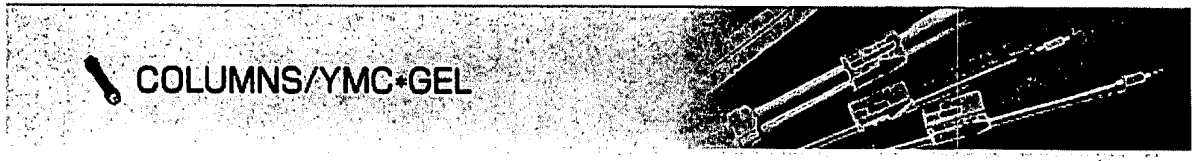

YMC-Pack SIL

>Product Information >Product list

High-Purity, High-Sample Recovery

The high purity silica found in YMC-Pack Silica columns provides virtually complete sample recovery.
The absence of silica impurities reduces non-specific sample adsorption which lowers sample recovery and may cause unusual peak shapes.

High Sample Loading, High Mechanical Stability

The totally porous nature of the silica found in YMC-Pack columns provides high sample loading. With some competitive silicas, the level of porosity would make the particles prone to fracture, resulting in fines and high backpressure. However, the high chemical purity of YMC*Gel Silica results in a particle structure with high mechanical strength.

POINT

- Choice of 60Å, 120Å, 200Å and 300Å pore size packings
- High Mechanical stability
- Ultra high-purity silica
- Available in analytical, semipreparative, preparative and

SPECIFICATION

Particle size	:3μm,5μm :10μm
Pore size	:60Å,120Å, 200Å,300Å
Usable pH range	:2.0-7.5

APPLICATION DATA

- Tocopherols
- Hydrocortisone and prednisone

process scale column sizes

YMC-Pack SIL	YMC-Pack CN	YMC-Pack Diol-NP
YMC-Pack Polyamine II	YMC-Pack NH2	YMC-Pack PA

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